The inclusion of physicians'attributes is critical for discrete choice experiments. This study identifies some statistically significant attributes such as the referral process. It confirms previous results by Miele, Weiland and Dungan (2012) showing how patient can benefit from reduction in HbA1C with centralized referral. Further development investigates how significant physicians' attributes can impact reversed conjoint modeling results on physicians' cost sensitivity.

PRM62

INCORPORATING A PHARMACOMETRIC MODEL-BASED META-ANALYSIS INTO A HEALTH ECONOMIC MICROSIMULATION MODEL OF COPD

Slejko JF[1], Ribbing J[2], Willke RJ[3]
[1]*University of Washington, Seattle, WA, USA,* [2]*Pfizer, Silverdal, Sweden,* [3]*Pfizer, Inc., New York, NY, USA*

OBJECTIVES: The study objective was to utilize a pharmacometric model-based meta-analysis (PMBMA) within a health economic microsimulation model (HEMM) of chronic obstructive pulmonary disease (COPD). PMBMA is a type of meta-regression which employs non-linear models estimated on trial-level data to relate patient and trial characteristics, dosing, surrogate markers, and outcomes effects of treatment. **METHODS:** A Markov microsimulation model was developed to estimate monthly changes in the key disease severity metrics of COPD (FEV1 and exacerbations) in order to compare a hypothetical drug that increases FEV1 to usual care. The PMBMA was used to predict a baseline exacerbation rate in a group of actual trial patients, given their known baseline FEV1. The hypothetical drug increased baseline FEV1, thereby decreasing the exacerbation rate in the hypothetical drug arm vis-à-vis the individual PMBMA predictions. Individual patient microsimulations and model memory allowed the rate monthly FEV1 decline to vary by patient and by month allowing for stochastic improvements. Validation of trial-level PMBMA estimates used in predictions was performed. Issues of synchronizing non-COPD mortality and common random numbers in microsimulation models were addressed. **RESULTS:** In a sample of 376 trial patients with a mean FEV1 (percent predicted) of 55%, had an exacerbation rate of 0.7 exacerbations per year, as predicted by the PMBMA. A drug that increased FEV1 at baseline by 30 mL resulted in a 21% decrease in exacerbations, while a 50 mL increase resulted in a 26% decrease. Given a simplified estimation of costs and QALYs associated with COPD, a drug with a 50 mL increase costing 40 Euro per month had an ICER of 46,736 Euro/QALY. **CONCLUSIONS:** The synergistic aspects of PMBMA and HEMM are highlighted in this hypothetical example. Markov microsimulation modeling allows the finer predictions of PMBMA to inform parameters while individual simulations allow advantages of model memory.

PRM63

A GUIDE ON HOW TO SPEEDUP COMPUTATION TIME IN CE-MODELS USING VBA OR MULTI-PROCESS PROGRAMMING IN C++

Khorshid M, Thuresson PO, Ray J
F. Hoffmann-La Roche Ltd., Basel, Switzerland

OBJECTIVES: There is a trend of health economic models (HEM) becoming computationally expensive. Additionally, less complex HEMs increasingly include some type of computationally demanding analysis like value of information (VOI; e.g. EVPI, EVPPI). However, the computation time required to perform such analyses are often stated as the primary constraint. Our objective was to determine whether efficiency could be achieved using programming languages and multi-process programming to substantially speedup the simulation time for HEMs. **METHODS:** Two different techniques were applied, firstly an implementation solely in VBA, secondly parallel computing implementation in C++. The general complexity of VOI-analysis in HEMs algorithms is due to nested loops. Multi-process programming is suitable for these tasks as it decomposes complex routines into small parts which are solved concurrently. A publicly available hip-replacement Markov model in Excel® served as a blueprint. It was reconstructed using the two aforementioned techniques, both replicas used the spreadsheet application as the interface, but calculations were performed in their respective programming environments. The computational time required to perform the EVPPI-analysis for each one of these techniques were compared. All computations were performed in an identical computational environment. Outcomes were compared to ensure there were no systematic differences in the underlying calculations. **RESULTS:** The VBA implementation of the hip-replacement model reduced simulation time by up to 7X compared to the original model. The improvement for the multiprocessing in C++ was 10X compared to the VBA implementation when running on a quad-core environment. **CONCLUSIONS:** This study demonstrated that the computation time of the selected HEM was improved considerably using the same language, primarily by minimizing the communication between VBA and spreadsheet. A more substantial improvement (~70X) was gained when using the multiprocessor capabilities in C++ combined with machine-level optimization. However, to achieve this speedup, more development time and may accompany reluctance due to specialist programming expertise.

PRM64

A MODEL SIMULATING EXTERNAL REFERENCE PRICING TO SUPPORT POLICY DECISION MAKING IN EUROPE

Vataire AL[1], Cetinsoy L[2], Rémuzat C[3], Aballea S[3], Toumi M[4]
[1]*University of Lyon 1, Villeurbanne, France,* [2]*Creativ-Ceutical, PARIS, France,* [3]*Creativ-Ceutical, Paris, France,* [4]*University Claude Bernard Lyon 1, Lyon, France*

OBJECTIVES: The objective of this project was to build a model simulating the external reference pricing (ERP) process, applied to the 28 European Union Member States, Iceland, Norway and Switzerland, to understand the price dynamics of ERP-based systems and predict the consequences of various ERP policy scenarios. **METHODS:** A discrete-event simulation (DES) modelling approach was adopted. This approach allowed for fixed ERP rules and quick dynamic changes. Three groups of attributes were included in the model: ERP policy attributes, drug attributes and countries' economic attributes. Occurrences of the following events were simulated: drug launch and first price setting, pricing decisions using ERP in different countries, exchange rate fluctuations, country's attributes modification, and drug price changes. Each price evaluation event implied the calculation of a new drug price and the model generated drug price evolution in each country over time. Model inputs were obtained from a literature review and consultation of representatives of competent authorities and international organizations. The model was validated by assessing actual drug prices at launch and over time for 53 randomly selected medicines. This model was developed for the EU Commission. **RESULTS:** The model could be used to assess the impact of pricing policies. For example, it showed that the price erosion predicted under the effects of ERP only was for most products slower than observed in reality, and thus that price negotiations also importantly contributed to price erosion. It can also be used to compare alternative launch sequences. The simulated price trends over time were consistent with observed trends. **CONCLUSIONS:** This DES model is the first comprehensive ERP published model across drug life cycle that allows testing various policy scenarios and predict impact of ERP in the real-life. This flexible model may prove useful tool to support decision making from the perspective of authorities or industry.

PRM65

REVIEW OF MODELS USED IN ECONOMIC ANALYSES OF NEW ORAL TREATMENTS FOR TYPE 2 DIABETES MELLITUS

Asche C[1], Eurich DT[2], Hippler S[1]
[1]*University of Illinois, Peoria, IL, USA,* [2]*University of Alberta, Edmonton, AB, Canada*

OBJECTIVES: This study aimed to provide insight into the utilization of cost-effectiveness modeling methods. The focus of our study was aimed at the applicability of these models, particularly around the major assumptions related to the clinical parameters used in the models, and subsequent clinical outcomes. **METHODS:** MEDLINE and EMBASE were searched from 1 January 2004 to 14 February 2013 in order to identify published cost-effectiveness evaluations for the treatment of T2DM by new oral treatments (GLP-1 receptor agonists and DPP-4 inhibitors). Once identified, the articles were reviewed and grouped together according to the type of model and study comparators. **RESULTS:** A total of 15 studies were identified in our review. Nearly all of the models utilized a health care payer perspective and provided a lifetime horizon. The CORE Diabetes Model, UKPDS Outcomes Model, Cardiff Diabetes Model, CDC Diabetes Cost- Effectiveness Group Model and Diabetes Mellitus Model were cited. Nearly all of the studies made significant assumptions surrounding the impact of GLP-1 receptor agonists or DPP-4 inhibitors on clinical parameters and subsequent short- and long-term outcomes. The impact of these clinical changes often resulted in large lifetime changes in health outcomes in the models. The validity of these projections, particularly for the longer time frames, is questionable. **CONCLUSIONS:** Future models should aim to include all relevant treatment outcomes, whether these relate to effects on underlying diabetes and its complications or to short- or long-term side effects of treatment. We need to explore why cost-saving interventions could benefit further from adding patient characteristics, which may be able to better predict the use of lower-cost alternatives. Moreover, the vast array of different clinical, cost and utility data used in the different models reviewed makes it apparent that a uniform methodology should be developed for diabetes economic models.

PRM66

ESTIMATING THE TIME TRADE-OFF VALUES OF THE EQ-5D-5L HEALTH STATES IN URBAN CHINA

Luo N[1], Liu G[2], Li M[3]
[1]*National University of Singapore, Singapore, Singapore,* [2]*Peking University, Beijing, China,* [3]*University of Maryland School of Pharmacy, Baltimore, MD, USA*

OBJECTIVES: The EQ-5D-5L is a new health-state classification system consisting of five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression), with each dimension described into five problem levels (no, slight, moderate, severe, and extreme). This study aimed to estimate the time trade-off (TTO) values of the 3,125 EQ-5D-5L health states to urban residents in China. **METHODS:** The values for 86 selected EQ-5D-5L health states were elicited using the 'composite' TTO technique from a general population sample (n=1,250) drawn from 5 Chinese cities. In computer-assisted personal interviews, participants each valued a randomly selected block of health states (n=10). Various function forms were constructed to specify the possible relationship between TTO values and health-state characteristics and estimated using linear regression models. The function form exhibiting the best fit of the data and the least prediction biases was identified to estimate the values of all EQ-5D-5L health states. **RESULTS:** The Hausman test suggested that random effects estimator was more efficient than fixed effects estimator for all function forms. The best model comprised a constant and twenty-one dummy variables indicating the presence or absence of specific problems or patterns of problems in a given EQ-5D-5L health state, including nineteen for all individual health problems except for slight anxiety/depression, one for severe or extreme problems in any functional dimensions, and one for the 5 mildest EQ-5D-5L health states. According to the final model, the mean absolute error of the predicted values for the 86 health states was 0.032 and the range of all the predicted values was -0.339 to 0.893. **CONCLUSIONS:** Values of EQ-5D-5L health states can be estimated using time trade-off values of a small portion of the health states. The EQ-5D-5L preference values estimated in this study may be used as quality-of-life weights in cost-utility analysis of health technologies and programs in China.

PRM67

IDENTIFYING AND CHARACTERIZING TRAJECTORIES OF QOL IN PERSONS WITH ADVANCED CANCER: IMPORTANT CONTRIBUTORS TO DECREASING QOL IN PEOPLE WITH CANCER

Rodriguez AM, Gagnon B, Mayo NE
McGill University, Montreal, QC, Canada

OBJECTIVES: In cancer, we aim at maintaining the Quality of Life (QOL) of patients. Yet minimal work examines predictors of QOL constructs over time. The aim of this study was to explore the temporal sequence leading to optimal QOL over time of key

components of the Wilson Cleary Model. **METHODS:** 212 persons with a variety of advanced cancer from the McGill University Health Center (MUHC) were evaluated using nine patient-reported outcomes and seven direct measures over a course of 18 months. As an attempt to minimize measurement error, Rasch measurement was used to model symptoms, function, general health perceptions (GHP), and overall quality of life (QOL) latent constructs. Additionally, biological variables were measured. The latent QOL construct was then modeled over time using "group-based modeling". Probability of group membership was finally predicted using the different biological, symptoms, function, and GHP constructs of the Wilson-Cleary model at study entry, which coincided with the time of cancer diagnosis. **RESULTS:** The Rasch QOL model over time resulted in 5 distinct trajectories: a linear increasing trajectory representing 26% of the sample, two flat medium and high trajectories representing 26 and 17% respectively, a quadratic increasing trajectory representing 25% of the sample, and a linear decreasing trajectory representing 5% of the sample. The latent constructs from the time of diagnosis that statistically significantly predicted membership in a QOL trajectory were age, sex, cancer type, recalled weight loss, CRP, social support, emotional status, and fatigue. **CONCLUSIONS:** Using Rasch, group-based trajectory modeling, and linear regression, we were able to discriminate between relevant QOL subgroups of patients. Most importantly, we were able to predict QOL trajectory from the time of diagnosis with advanced cancer. This enabled us to make preliminary conclusions about the most important contributors to QOL over time, and emphasize the importance in assessing these constructs in people with cancer.

PRM68

BIAS WHEN ADJUSTING FOR SURROGATES OF CONFOUNDERS

Page JH, Chia VM

Amgen, Inc, Thousand Oaks, CA, USA

OBJECTIVES: High-dimensional propensity score (HDPS) methods have been used in health care claims data in an attempt to control confounding by adjusting for a large number of covariates that may be proxies for unobserved factors. We have previously shown that PS models are biased with non-linear link functions. We conducted a Monte Carlo simulation study to understand whether inclusion of covariates that are children of unmeasured confounders and other unmeasured parents of the outcome variable (colliders) may bias the relationship between exposure and outcome by estimating mean bias, and standard errors. **METHODS:** We used directed acyclic graphs to replicate the causal network of plausible confounding scenarios. We simulated a scenario where the outcome variable Y is a function of a confounder, C, and another parent, U, but not of exposure X (function of C). Covariate Z is a function of parents C and U. All variables had normally distributed random errors. We conducted Monte Carlo simulations of the causal network, with varying strengths of each of the causal relations, and estimated the effect of X on Y, using linear regression models, while adjusting for covariate Z. **RESULTS:** Correctly specified models were unbiased. Bias was large in models with X only (bias 1.5 with variable standard errors). There was some reduction in bias in some situations where Z was highly correlated with the confounder, C, but increased bias when much of the variance in Y was determined by U. **CONCLUSIONS:** Adjustment for colliders that are children of unmeasured determinants of the outcome variable, but not of the exposure, may also increase bias. This is of great importance in observational studies, particularly when using HDPS to adjust for large numbers of variables that are not true confounders. Researchers should always use causal knowledge when using data to make causal inference.

PRM69

SIZE DISTORTION OF HYPOTHESIS TESTS FOR TWO-STAGE LEAST SQUARES MODEL: WHAT THE RULE OF THUMB CAN'T GIVE YOU?

Shao H, Shi L

Tulane University, New Orleans, LA, USA

OBJECTIVES: Big data approaches may lead to multiple strong instrumental variables (IV), significantly improving the performance of two-stage least squares model (TSLS). The current rule of thumb for detecting weak IV is based on the goal of keeping relative bias of TSLS less than 0.1. With the increasing number of IVs, we need to examine the impact of week IV on hypothesis testing. We investigated whether or not the rule of thumb can be efficient enough to prevent size distortion of hypothesis testing for TSLS? **METHODS:** We used a Monte Carlo approach to create 28 original data sets for different models with the number of IVs varying from 3 to 30. For each model, we created 2000 observations and conducted 50,000 iterations to reach a converged outcome. The relationship between the endogenous variable and IVs was carefully adjusted to let the F statistics for the first stage model equal 10 (rule of thumb). The mean value of relative bias and percent of false rejection for each model were recorded and compared across all the models. **RESULTS:** The relative bias of TSLS equaled 0.1 constantly across all the models in the study. However, the likelihood of rejecting a true hypothesis increased when the number of IVs in the model increased while holding the F statistics for the first stage model equal to 10. And this likelihood exceeded 10% when TSLS had 24 IVs and exceeded 15% when TSLS had 30 IVs. **CONCLUSIONS:** When more IVs were added into the TSLS model, the rule of thumb was no longer an efficient guarantee for good performance in hypothesis testing. A more restricted margin for F statistics is needed to be explored to improve the rule of thumb, especially when the number of IVs could be large in the context of big data.

PRM70

DEPRESSION AND COMORBID OBESITY AND HYPERTENSION IN UNITED STATES CHILDREN

Tevie J[1], Shaya FT[2]

[1]*University of Maryland, Baltimore, MD, USA,* [2]*University of Maryland School of Pharmacy, Baltimore, MD, USA*

OBJECTIVES: To investigate the association between depression and comorbid obesity and hypertension in US children over a 8-year period using data from the National Health and Nutritional Examination Survey among those with depression or hypertension. **METHODS:** We built a logistic regression model using a sample of 727 respondents aged 0-18 between 2005 and 2012. **RESULTS:** Out of 727 subjects, 49.2% were female, 50.1% were male, 11.5% were between the ages of 0-5, 37.8% between the ages of 6-10, 26% between the ages of 11-15, 24.5% between the ages of 16-18, 28.7% were White, 71.3% were non-White,16.4% were obese and 3.6% had hypertension. Obesity and hypertension are significant predictors of depression. Children who are obese are about 2.9 times more likely (p=0.005) to be depressed than children who are not obese, and children who suffer from hypertension are approximately 4.6 times more likely (p<0.001) to experience depression than those who do not have hypertension. Other significant predictors of depression in children are gender (p<0.001; OR=0.486) and family size (p=0.06; OR=0.673). **CONCLUSIONS:** Obesity and hypertension are associated with depression after controlling for other factors. This finding has important implications for depression management in children. It brings into focus the maintenance of a healthy body mass index (BMI) in mitigating depression.

PRM71

ANXIETY AND COMORBID OBESITY AND HYPERTENSION IN UNITED STATES CHILDREN

Tevie J[1], Shaya FT[2]

[1]*University of Maryland, Baltimore, MD, USA,* [2]*University of Maryland School of Pharmacy, Baltimore, MD, USA*

OBJECTIVES: To investigate the association between anxiety and comorbid obesity and hypertension in US children over a 8-year period using data from the National Health and Nutritional Examination Survey among those with anxiety or hypertension. **METHODS:** We built a logistic regression model using a sample of 717 respondents aged 0-18 between 2005 and 2012. **RESULTS:** Out of 717 subjects, 49.2% were female, 50.1% were male, 11.5% were between the ages of 0-5, 37.8% between the ages of 6-10, 26% between the ages of 11-15, 24.5% between the ages of 16-18, 28.7% were White, 71.3% were non-White,16.4% were obese and 3.6% had hypertension. Obesity is a significant predictor of anxiety. Obese children are about 2.1 times more likely (p=0.0002) to suffer from anxiety compared with children who are not obese. A significant association was also found between anxiety and gender (p=0.05; OR=0.341) and family income (p=0.06; OR=1.012). **CONCLUSIONS:** Obesity predicts the prevalence of anxiety in children. The implication is that maintaining a healthy body mass index (BMI) in children could significantly reduce the prevalence of anxiety in children.

PRM72

THE IMPACT OF TWO DIFFERENT CASE DEFINITIONS OF MAJOR CONGENITAL MALFORMATIONS IDENTIFIED FROM QUEBEC (CANADA) ADMINISTRATIVE DATABASES ON THEIR ASSOCIATION WITH ASTHMA CONTROLLER MEDICATIONS TAKEN DURING PREGNANCY

Eltonsy S, Blais L

University of Montreal, QC, Canada

BACKGROUND & OBJECTIVES: Accurate identification of major malformation cases from administrative databases is crucial for perinatal epidemiology. In Quebec, most of major malformations are detected in hospital, however administrative databases capture diagnoses data from both hospitals and other medical facilities. We aimed to compare the prevalence of major congenital malformations identified from administrative databases diagnostic codes (ICD-9 and ICD-10) with 2 definitions: diagnoses made in hospital only vs. diagnoses made in hospital and other medical facilities. We further evaluated the impact of using each definition to quantify the association between maternal use of asthma controller medications and the prevalence of major malformations at birth and during the first year of life. **METHODS:** A cohort of pregnancies from asthmatic women between 1990 and 2010 was formed through the linkage of administrative databases from Quebec. We calculated the prevalence of major malformations identified in the 1st year of life of the newborn using the 2 case definitions. We also calculated the crude odds ratio (OR) of major malformations associated with maternal use of inhaled corticosteroids (ICS) and long-acting beta$_2$-agonists (LABA) in the 1st trimester of pregnancy. **RESULTS:** From 30655 pregnancies, 2090 (6.8%) major malformations were identified with hospital diagnostic codes only vs. 2748 (9.0%) with hospital and other medical facilities diagnostic codes. The OR of major malformations associated with ICS was 1.1 (95%CI: 1.0-1.2) with the first and 1.1 (95%CI: 1.0-1.2) with the second case definition. Corresponding results were 1.3 (95%CI: 1.0-1.6) and 1.1 (95%CI: 0.9-1.4) for LABA exposure. **CONCLUSIONS:** The case definition of congenital malformations had a considerable impact on the prevalence of major congenital malformations, but less impact on the associations we examined. The percentage of false positive cases when using all medical facilities diagnostic codes in the case definition is unknown and should be the objective for future research.

PRM73

SURVIVAL MODELING FOR THE ESTIMATION OF TRANSITION PROBABILITIES IN MODEL-BASED ECONOMIC EVALUATIONS IN THE ABSENCE OF INDIVIDUAL PATIENT DATA: A TUTORIAL

Diaby V[1], Adunlin G[1], Montero A[2]

[1]*Florida A&M University, Tallahassee, FL, USA,* [2]*Cleveland Clinic, Clevland, OH, USA*

OBJECTIVES: Survival modeling techniques are increasingly being used as part of decision modeling for health economic evaluations. As many models are available, it is imperative for researchers to know about the steps in selecting and using the most suitable ones. This paper is aimed at proposing a tutorial for the application of appropriate survival modeling techniques to estimate transition probabilities, for use in model-based economic evaluations, in the absence of individual patient data. The use of the proposed tutorial is illustrated based on the final progression-free survival (PFS) analysis of BOLERO-2 trial in metastatic breast cancer (mBC). **METHODS:** An algorithm was adopted from Guyot and colleagues, and was then run in the statistical package R to reconstruct individual patient data (IPD), based on the final